

Proposed Human Toxicity Estimates for Several Toxic Industrial Chemicals (TIC)

Douglas R. Sommerville, PE ¹, Stephen R. Channel, DVM, MS, DABT ², Sandra Mendez ³, John J. Bray ³
(1) U.S. Army Edgewood Chemical Biological Center, (2) Leidos, Inc., (3) OptiMetrics, Inc.

Abstract

A toxic industrial chemical/toxic industrial material (TIC/TIM) task force had been established to provide TIC prioritization and baseline TIC acquisition capability requirements and recommendations to the Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD). These requirements and recommendations are intended for use by the CBD Program during routine military operations outside the continental United States. They are not intended for civil response planning. ECBC has developed proposed human inhalation (IH) toxicity estimates for chemicals of interest to the task force. The project was designed to be a focused and expeditious assessment and not a comprehensive “all source” literature capture and analysis. The project took advantage of the extensive literature searches conducted by the National Research Council during the development of acute exposure guideline levels (AEGLs) for individual chemicals.

In Phase I, lethal and severe effects IH toxicity estimates were produced for 17 selected chemicals: ammonia, chlorine, cyanogen chloride, formaldehyde, hydrogen bromide, hydrogen chloride, hydrogen cyanide, hydrogen fluoride, hydrogen sulfide, mercury vapor, methyl bromide, nitric acid, nitrogen dioxide, octamethyl pyrophosphoramide, phosgene, sulfur dioxide, and sulfuric acid. The 2 minute median effective dosages, probit slopes (PS), and toxic load exponents (TLE) are reported for 16 of these chemicals. After Phase I, DTRA sponsored an extension of the project in support of their reachback capability.

In Phase II, an additional 26 TICs were selected for review and development of toxicity estimates: acrolein, acrylonitrile, allyl alcohol, arsine, boron trifluoride, carbon monoxide, diborane, diisopropyl fluorophosphates (DFP), dimethylhydrazine, dimethylamine, ethylene oxide, fluorine, hydrazine, hydrogen selenide, monomethylamine, methyl hydrazine, methyl isocyanate, methylphosphonic difluoride (DF), O-Ethyl-O’-(2-diisopropylaminoethyl) methylphosphonite (EDMP or QL), parathion (ethyl and methyl), phosphorous oxychloride, phosphorous trichloride, propylene oxide, sulfur trioxide, and uranium hexafluoride. Prior to this effort, very few median effective dosages/probit slopes/TLE appropriate for military casualty estimates existed for any of the TICs reviewed.

Purpose, Product and Requirements

Purpose: Develop human IH toxicity estimates for military operations for several TICs.
Final Product: Median effective dosages (EC_{t50} & LC_{t50}), PS & TLE for lethality & severe effects from IH exposures.
Prior to Present Effort: Military TIC estimates suitable for casualty estimation for acute exposure scenarios did not exist (in general). Civilian estimates (threshold) were inappropriately used instead (such as AEGLs).
General Requirement:
Toxicity estimates are needed to translate vapor concentration—time (C-t) profiles into percent probability of effect on exposed personnel as part of the operational hazard analysis (OHA) process.
Specific CBD Program Requirements for Military TIC Estimates:

- Preparation of formal requirements for development/ production/testing of a wide variety of Chemical, Biological, Radiological and Nuclear (CBRN) related equipment (for JPEO-CBD).
- Accurate threat assessments of military release scenarios (for DTRA Reachback).

Benefits and Impact

Toxicity estimates suitable for casualty estimation (both civilian & military) for acute exposures did not exist for TICs (for the most part) prior to current effort.

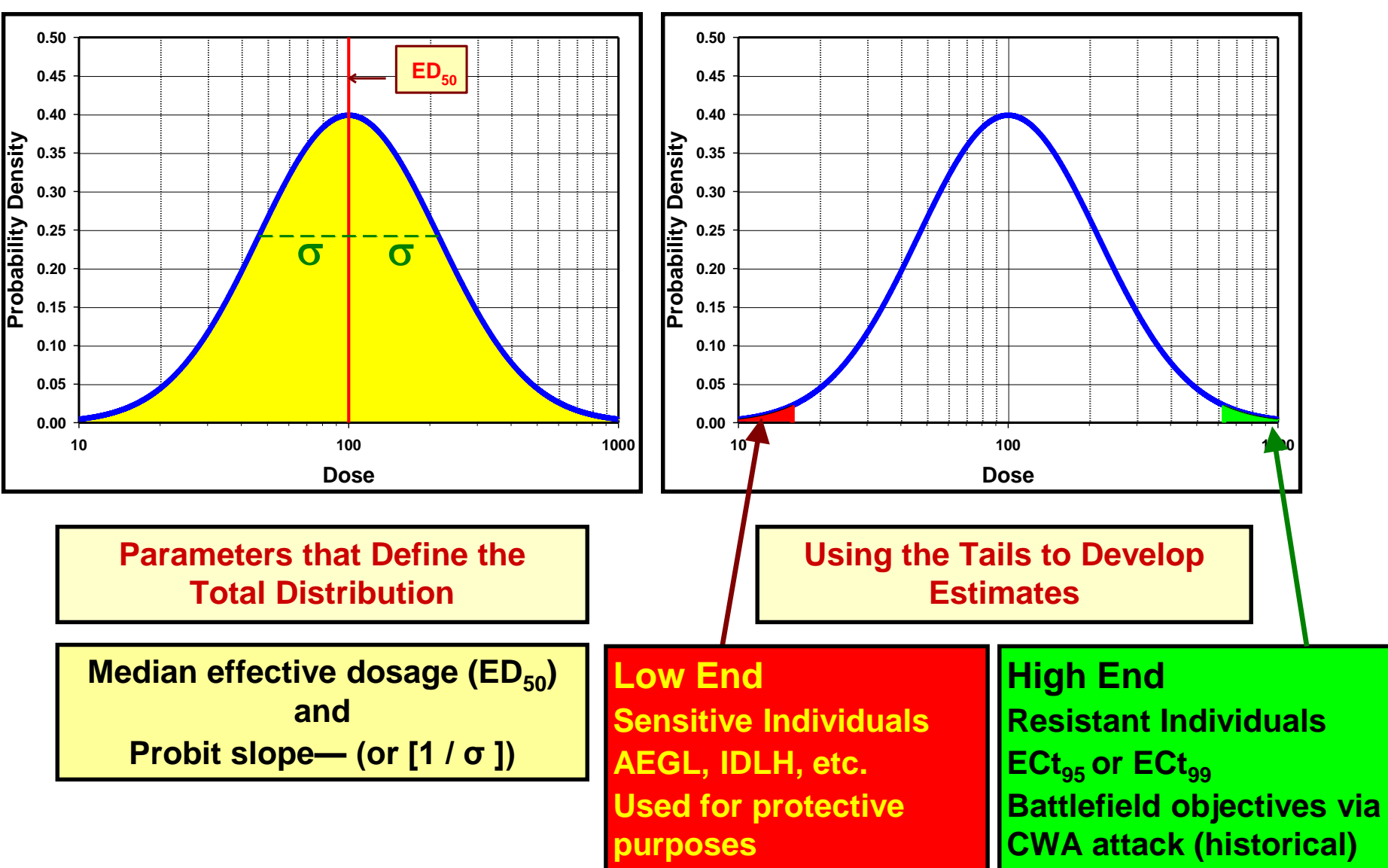
- Whole dose response (DR) curve needs to be defined for casualty estimation to be possible.
- Previous TIC estimates (ex. AEGLs) mostly for threshold (1% effect) levels and developed to protect sensitive populations

Now possible (for TICs addressed) to properly balance risk and consequences of toxic exposure against other factors.

- Chemical warfare agent detectors--false alarm rates, speed of detection, etc.
- Protective equipment--heat and respiratory stress, reduced field of vision and motion, etc.
- Decontamination--what is clean enough?

More realistic and accurate threat assessments for military release scenarios.
Military estimates can be used as starting point for civilian estimates appropriate for casualty estimation.

The Bell Curve, Population Basis and Toxicity Estimates



Civilian versus Military Populations

Property	General Population	Military Subpopulation
Purpose of Estimates	Protective	Predictive
DR Curve Used in Estimate	Tail (Low End)	Whole curve
Risk Acceptance	Very Low	Mission Dependent (Varying Degrees)
Avoidance Options	Evacuation or Shelter-in-Place	Mission trumps avoidance
Protective Gear Available	Little to none	Gas masks, MOPP gear, etc.
Protective Gear Training	Little to none	Extensive
Medical Screening	Varies widely	Extensive for all
Chronic conditions	Large Incidence	Small Incidence

Source Material for Military Toxicity Estimates—AEGL TSD

AEGL Technical Support Document

- National Advisory Committee for Acute Emergency Guideline Limits (NAC/AEGLs)
- Provide threshold evacuation limits for civilian populations for 10 min, 1, 4, and 8 hrs exposures

What Goes into an AEGL TSD?

- All possible toxicity open data sources are searched and evaluated by a committee of subject matter experts
 - Exact sources specified by NRC (2001)
 - Sources include public and industry publications as well as electronic databases (RTECS, DTIC, etc.)
 - Major limitation is lack of access to documents not releasable to the public
 - This is an issue for TICs that were formal CW agents—many government documents were not available to the AEGL committee
- TSDs have been thoroughly peer reviewed in public settings and generally include all applicable open source literature

How were the TSDs Used?

- Given specified time and budget restraints, it is reasonable to use the NRC’s AEGL Committee to “vet” the literature
- Only material used/cited in a TIC’s TSD were consulted
 - Exceptions made for former CW agents (ex. phosgene)—readily available government technical reports were used on case-by-case basis
- Assumed AEGLs equivalent to the 1% response level for the general population (implicit in the AEGL SOP)
 - AEGL-3 → LC₀₁
 - AEGL-2 → EC₀₁ (severe)

If TSD not Available for TIC

- Borrowed work from other sources (ex. CSAC report on cyanogen chloride)
- Performed own literature search using same databases as AEGL Committee and DoD sources
 - Sufficient data available—generate estimates (ex. DFP and DF)
 - Insufficient data available—recommend no estimates be made (ex. OMPA and EMPTA)

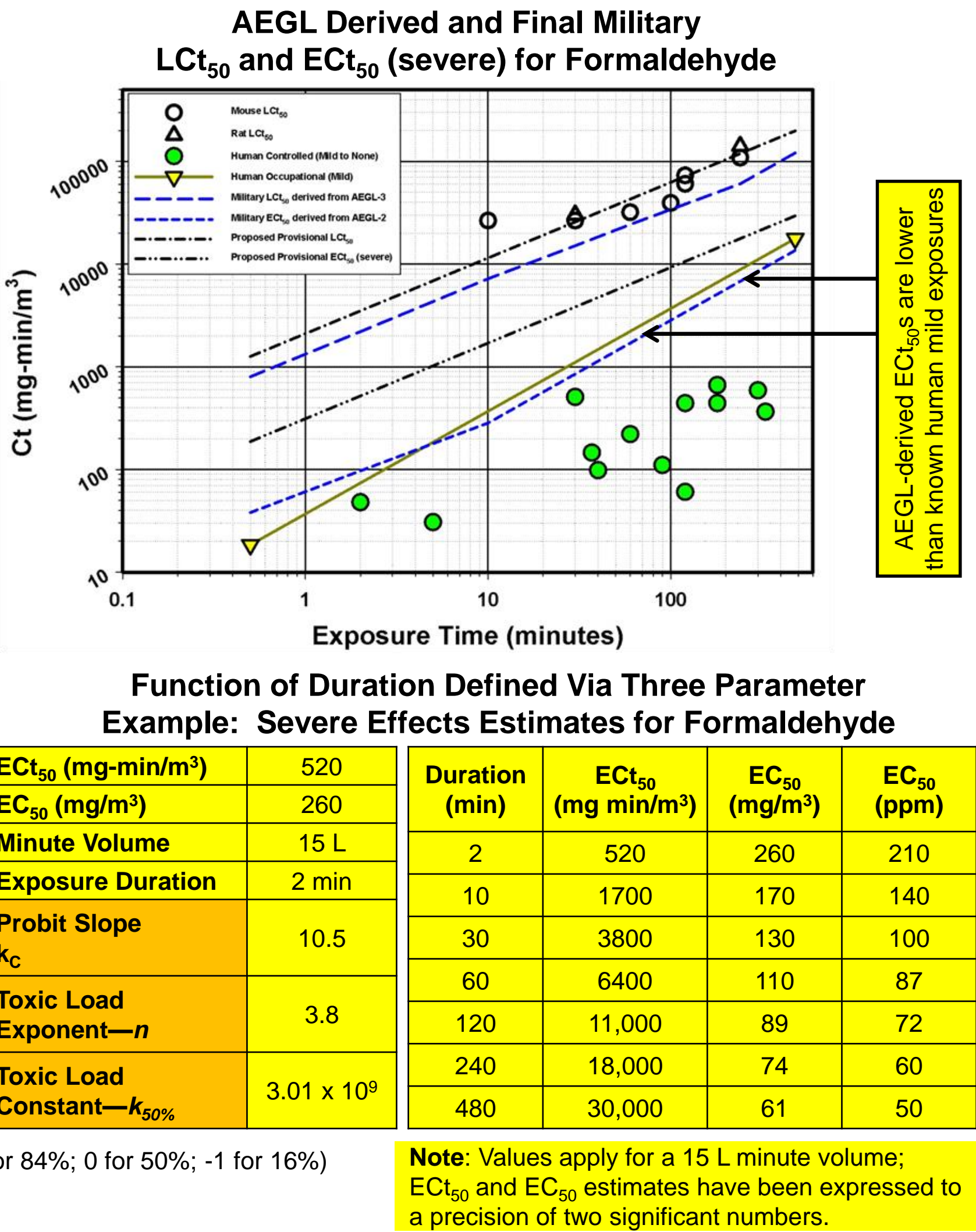
General Approach

- Initial estimates (AEGL Derived Values)
 - Convert AEGL-3 and AEGL-2 into military LC₀₁ and EC₀₁ (severe) via removal of uncertainty factors (UF)
 - Use TSD PS estimate to LC₀₁ and EC₀₁ (severe) into 50% effect values
- Are AEGL endpoints compatible against military operational endpoints?
- Comparison with known mammalian and human exposures—does AEGL Derived Values make sense?
- Augment TSD with source or additional data
 - DoD technical documents from DTIC
 - ECBC institutional knowledge
 - DHS CSAC reports
- Development of final estimates
 - Statistical analysis
 - Scaling from animal to human
 - Occupational/accidental human exposures
 - Default approaches for limited data situations
 - Institutional knowledge and personal experience of authors—does it make sense at the end of the day?
 - Peer review of methods and results

$$E(C^t)_{xx} = k_{50\%} \text{ antilog} \left[\frac{nZ}{k_c} \right]$$

Z – normits corresponding to XX percent effect (1 for 84%; 0 for 50%; -1 for 16%)

Method and Results



Acknowledgments and References: The authors thank the JPEO-CBD (Phase I) (POC: Karen McGrady) and the Defense Threat Reduction Agency/Joint Science and Technology Office (Phase 2/CB3607) for their assistance and funding for this work. Funding for a parallel effort (results incorporated into JPEO-CBD/DTRA effort) was sponsored by DHS Chemical Security Analysis Center (CSAC) (POC: George Famini & Rachel Gooding). The views expressed in this presentation are those of the authors and do not necessarily reflect official policy or the position of the Department of Defense or the U.S. Government.
We also acknowledge the valuable advice and assistance provided by Jerry Glasow (DTRA), Ronald Crosier, Jared Lee, Carolyn McClellan, Kyong Park and Sharon Reutter-Christy (ECBC), Marie Jefferson (Optimetrics).
References: Available upon request.



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